



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/751,703	01/05/2004	Darren R. Veach	2003080-0144 (SK-1028-US)	5361
24280	7590	11/17/2005	EXAMINER	
CHOATE, HALL & STEWART LLP TWO INTERNATIONAL PLACE BOSTON, MA 02110			MCKENZIE, THOMAS C	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/751,703	Applicant(s) VEACH ET AL.	
	Examiner Thomas McKenzie, Ph.D.	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 January 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 34-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19, 21-26, 28, 29 and 31-33 is/are rejected.
- 7) ☒ Claim(s) 20, 27 and 30 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/31/05</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This action is in response to an application filed on 1/5/04. There are forty claims pending and thirty-three under consideration. Claims 1-30 are compound claims. Claim 33 is a composition claim. Claims 31 and 32 are method of making claims. This is the first action on the merits. The application concerns some 2-amino-pyrido[2,3-d]pyrimidin-7(8H)-one compounds, compositions, and synthesis thereof.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C.

121:

- I. Claims 1-33, drawn to compounds and compositions, classified in class 544, subclass 279.
- II. Claims 34-40, drawn to cancer treatment, classified in class 514, subclass 264.11.

The inventions are distinct, each from the other because of the following reasons: inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case there are thousands

of distinct cancers. Thus, Applicants admit their compounds have thousands of different uses. In addition compounds unrelated to the present invention can treat many specific cancers. For example breast cancer can be treated the monoclonal antibody Herceptin. Thus both prongs of the test are met.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Hunter Baker on 10/19/05 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-33. Applicant in replying to this Office action must make affirmation of this election. Claims 34-40 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or

allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See “Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b),” 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the examiner withdraws the restriction requirement before the patent issues. See MPEP § 804.01.

Priority

6. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. [1] as follows: the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/437,936, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The formula given in claim 1 of this provisional application supports $Cy = Ar$ but not the broader cyclic aliphatic, alkyl, cyclic heterocycle etc. In addition there is not complete support for all the presently claimed individual species.

The disclosure of the prior-filed application, Application No. 60/4500,978, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. This second provisional application uses the same generic formulas but adds a few additional species.

Thus, claims 6-18, 21, and 24-26 are awarded the effective filing date of the Application No. 60/437,936, 1/3/03. All remaining claims 1-5, 19, 20, 22, 23, and 27-33 are awarded the instant filing date 1/5/04.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6-10, 12-15, 17, 18, 21, 23-25, 28, 29, 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. throughout these claims in the definitions of Cy, Ro, Ar, N with a circle around it, and Ak, Applicants have the limitation that the various aliphatic, heterocyclic, aryl, heteroaryl etc. groups may be either "substituted or unsubstituted". Substituted by what? Lines 18-27, page 23 states that "all permissible substituent of organic compounds" without giving any specific substituents intended. Permissible to

whom and for what purpose? Are these limited to the "stable" compounds described in lines 20-27 on the same page? The term "permissible" is a relative term, which renders the claim indefinite. The term "permissible" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. In lines 9-21, page 25 there is a list of possible substituents. However, the passage uses the open terms "some examples" and "include, but are not limited to". What additional substituents, in addition to those listed are intended? The Examiner suggests listing the intended substituents in the claims, relying upon lines 10-16, page 25 for support.

8. Claims 1-4, 6-18, 21, 23-26, 28, 29, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "pharmaceutically acceptable derivatives thereof" is indefinite for we do not know which compounds are contemplated. A derivative is the result of a reaction upon an organic molecule. Since we do not know the reagents or the conditions of these reactions, there is no way of determining the structures of the claimed "derivatives". The phrase "derivatives thereof" is, in essence, a product by process claim. Yet Applicants have not described the intended processes

sufficiently that we may understand the structures of the compounds they claim. Webster's New World Dictionary defines derivative as "a substance derived from ... another substance by chemical change", and "substitution of one or more elements or radicals for one or more constituents of the original substance" has occurred. All implying that new chemical bonds have formed. Clearly, many of the "derivatives" obtained from compounds of formula I, will themselves be covered by formula I. The question is, what compounds falling outside the structural limitations of formula I are covered under the rubric of "derivatives"? Lines 19-25, page 30 given some indication of what is intended but uses open terms and gives no process by which these derivatives are to be made. the Examiner suggests replacing "derivatives" by "salts", being mindful of the enablement rejection discussed below.

9. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The variable n does not occur in parent claim 1 although it does occur in claim 2. Was dependence upon claim 2 intended? Or does variable "n" indicate the number of allowed substituents on Cy?
10. Claim 19 has the structure of SKI DV2-171 as the penultimate formula in this claim. The substituted benzyl group shown attached is not an Ar group as

defined in parent claim 6. There is insufficient antecedent basis for this limitation in the claim. Should not this compound depend upon claim 28?

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-18, 21, 23-26, 28, 29, and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making prodrugs, metabolites, "esters, salts of the esters, or any other adduct or derivative" of the claimed compounds. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry to use the invention. "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of

a claimed alcohol, for example, is in fact a prodrug, that produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism *de novo*, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be clinically effective. Determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation.

b) The direction concerning the prodrugs is found in lines 24-25, page 30. c) There is no working example of a prodrug of a compound presently claimed. d) The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the human body. e) Wolff (Medicinal Chemistry) summarizes the state of the prodrug art. The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic

issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modern Pharmaceutics) in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug. f) Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would have a Ph. D. degree and several years of industrial experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the hundreds of thousands of compounds presently claimed as well as the presently unknown list of potential derivatives embraced by the claims.

MPEP 2164.01(a) states, "[a] conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed.

Cir. 1993).” That conclusion is clearly justified here. Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

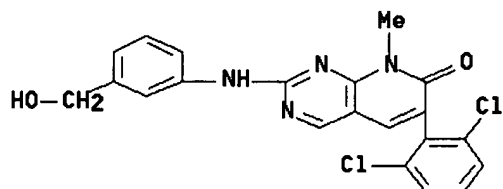
Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

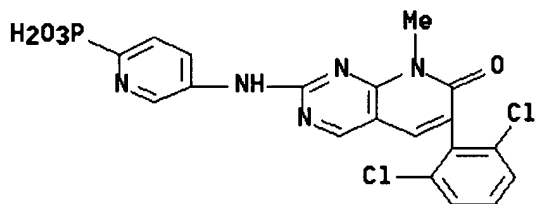
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4, 6-8, 10, 12-16, 21, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Netzer (WO 2003/057165 A2, cited by Applicants). The compound shown below fits the formula of claim 1 with X = chlorine and Cy or Ar = phenyl substituted with R_o = hydroxymethyl. It has Registry Number 185039-91-2 and is found in Fig. 20 of the reference. It is Compound 2. Another anticipatory compound is compound 1. Claim 99 of the reference teaches compositions. Thus, the present claim 33 is taught.



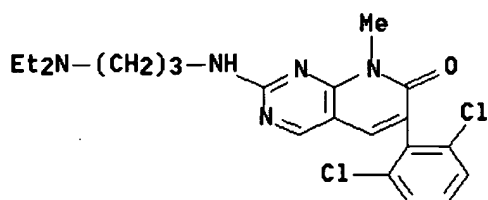
13. Claims 1, 3, 4, 6-8, 9, 10, 12-15, 17, 18, 24, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Weigele (WO 2001/044258 A1, cited by Applicants). There are fifteen compounds found in this reference, which anticipate Applicants claims. For example, the compound shown below fits the formula of claim 17 with X = chlorine and R_o = the acyl group phosphonic acid. It has Registry Number 344891-26-5 and is found in page 109 of the reference. It is Example 20 and its synthesis is described in the passage spanning line 26, page 108 to line 20, page 110.



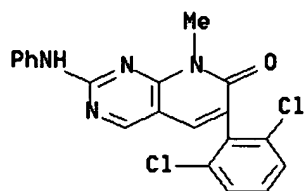
The *para* phenyl substituted compounds such as the one with registry number 344891-28-7 anticipate claims 8, 12-15, and 18. This compound is Example i-A and is pictured on page 72. Compositions of these compounds are taught in lines 6-9, page 19. Thus, the present claim 33 is anticipated.

14. Claims 1, 3, 4, 6-15, 18, 23, 28, 29, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Doherty ('422, cited by Applicants). There are sixteen compounds in this reference, which teach Applicants claims. For

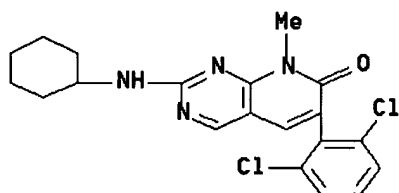
example, the compound shown below fits the formula of claim 28 with 1 with X = chlorine and Ak = propyl substituted with diethylamino. It has Registry Number 185039-31-0 and is found in lines 15-39, column 32 of the reference. It is Example 28. Thus, claims 28 and 29 are anticipated. The *ortho*-methoxyanilino and 3-aminopyridyl compounds are also taught. Thus, the present claims 1, 3, 4, 6-15, and 23 are anticipated. Compositions are taught in claim 10 of the reference. Thus, the present claim 33 is taught.



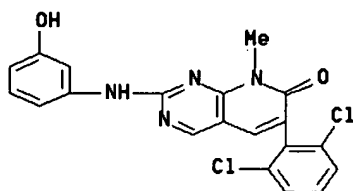
15. Claims 1-4, 6-16 18, 21-23, 28, 29, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Blankley ('914, cited by Applicants). There are sixty-two compounds in this reference that either anticipate or make obvious Applicants claims. For example, the compound shown below fits the formula of claim 6 with X = chlorine, Ar = phenyl, and R_o = hydrogen. Thus, the present claims 1, 3, 4, 6-8, 10-14, 18, 21, and 23 are anticipated. It has Registry Number 185039-63-8 and is found in lines 36-54, column 38 of the reference. It is Example 54.



The compound shown below fits the formula of claim 2 with X = chlorine and R_o = hydrogen. Thus, the present claims 1-4, 28, and 29 are anticipated. It has Registry Number 185039-63-8 and is found in lines 36-54, column 38 of the reference. It is Example 54.

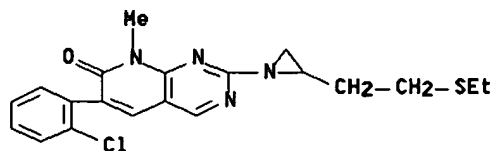


The compound shown below fits the formula of claim 6 with X = chlorine, Ar = 3-hydroxyphenyl, n = 1, and R_o = hydroxyl. Thus, the present claims 1-4, 28, and 29 are anticipated. It has Registry Number 185039-96-7 and is found in lines 41-60, column 49 of the reference. It is Example 87. Thus, claims 1, 3, 4, 6-8, 10, 12-16, and 21 are taught. It is identical to the compound that Applicants label SKI DV2-89. Thus, the present claim 22 is anticipated.



The various pyridylamino compounds taught in this reference anticipate the present claim 9. For example, the compound with registry number 185039-94-5 has Ar = 6-methoxy-3-pyridyl. Claims 22-26 of the reference teach compositions. thus, the present claim 33 is taught.

16. Claims 1-4, 25, 26, 28, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen (WO 2002/018380 A1, cited by Applicants). There are 88 compounds in this reference that anticipate Applicants' claims. For example, the compound shown below fits the formula of claim 25 with X = chlorine and hydrogen and N with a circle around it = 1-aziridiny1 substituted by 2-(ethylthio)ethyl. It has Registry Number 402740-62-9 and is found in lines 19-27, page 124 of the reference. It is compound 102B. Thus, claims 25 and 26 are taught. Claim 22 of the reference teaches compositions. Thus, the present claim 33 is anticipated. The compound 101, found in the lines 1-17, page 123 of the reference has Cy = cyclohexyl substituted by *trans*-4-methoxy. Thus, the present claims 1-4, 28, and 29 are taught.



Claim Rejections - 35 USC § 103

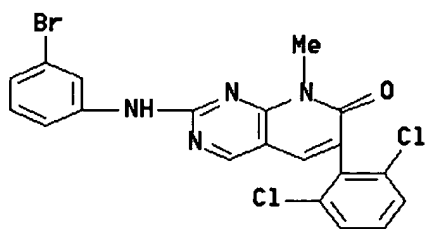
17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 18, 19, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Netzer (WO 2003/057165 A2, cited by Applicants) as applied above. The reference teaches the compound with registry number 185039-91-2 shown above. The Applicant claims the compounds with the hydroxymethyl group in the *ortho* and *para* positions of the anilino ring. The reference teaches a compound with a hydroxymethyl group in the *meta* position of this ring. The difference between the claimed and taught compounds is the position of attachment of the hydroxymethyl group. These are *per se* obvious ring position isomers and require no specific teaching. *In re JONES* 74 USPQ 152, *In re NORRIS* 84 USPQ 458, quoted with approval *Ex parte Ullyot* 103 USPQ 185, also quoted with approval *Ex parte BIEL* 124 USPQ 109, *Ex parte MOWRY AND SEYMOUR* 91 USPQ 219, *In re MEHTA*

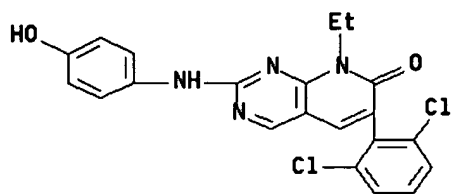
146 USPQ 284, *In re Wilder* 195 USPQ 426, quoted with approval *In re Grabiak* 226 USPQ 870. The substance that Applicants label SKI DV2-51 is the *para* isomer of the compound RN 185039-91-2. Thus, the present claim 19 is made obvious.

18. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blankley ('914, cited by Applicants). The reference teaches the compound with registry number 185039-64-9 shown below. The Applicant claims the compounds SKI DV2-53, which has a *para* bromine atom on the anilino ring. The reference teaches a compound with *meta* bromine atom. The compound shown in the reference in the passage spanning line 56, column 38 to line 9, column 39. It is Example 55. The difference between the claimed and taught compounds is the position of attachment of the bromine atom. These are *per se* obvious ring position isomers and require no specific teaching.

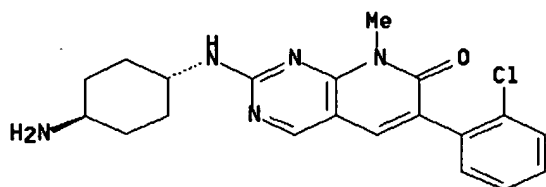


19. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blankley ('914, cited by Applicants). The reference teaches the compound with registry number 185039-84-3 shown below. The Applicant claims the compound

SKI DV2-47, which has a methyl group at N-8 of the pyrido[2,3-d]pyrimidin-7(8H)-one ring. The reference teaches a compound with an ethyl group at N-8. The compound shown in the reference in lines 15-49, column 45. It is Example 75. The difference between the claimed and taught compounds is the size of the N-8 substituent. Compounds that differ only by the presence or absence of an extra methylene group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methylene groups. See *In re Wood*, 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.



20. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chen (WO 2002/018380 A1, cited by Applicants). The reference teaches the compound with registry number 402926-10-7 shown below. The Applicant claims the compound SKI DV2-155, which has chlorines in the 2 and 6 positions of the phenyl ring at position C-6 of the pyrido[2,3-d]pyrimidin-7(8H)-one core. The reference teaches a compound with chlorine at the 2 position and a hydrogen at the 6 position of the phenyl ring. The compound shown in the reference in lines 1-15, page 51. It is compound 13. The difference between the claimed and taught compounds is the addition of the second chlorine atom to the taught compound. The suggestion to add this atom is found in claim 3 of the primary reference. This teaches that Ar¹, which corresponds to that ring, may be "substituted with one or two, preferably two halo". The skilled medicinal chemist would be motivated to add this chlorine atom to explore the SAR and to improve the metabolism characteristics of his compound.



21. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chen (WO 2002/018380 A1, cited by Applicants) as applied to claim 5 above, and further in view of Boschelli (J. Med. Chem.). In the first complete sentence on page 4366, the secondary reference says, "[i]n addition, a model of the binding of these two classes of pyrido[2,3-*d*]pyrimidines to the kinase domains of TKs proposed that modification of the group at C-6 could confer selectivity." In Table 2, page 4369 the greater potency of the 2,6-dichloro compounds 2a and 2b over their de-chlorinated analogues 28 and 54 in the FDFr and c-Src kinase assays would motivate the skilled medicinal chemist to add the second chlorine at position 6 to the compound taught in the primary reference. This would be done to improve the selectivity and potency of the compound.

Allowable Subject Matter


22. Claims 31 and 32 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims. Claims 20, 27, and 30 are objected to as being dependent upon a rejected base

claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

23. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

24. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (571) 273-8300. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 9:00am to 5:30pm, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, acting SPE of Art Unit 1624, at (571)-272-0661.


Thomas C. McKenzie, Ph.D.
Primary Examiner
Art Unit 1624
(571) 272-0670

TCMcK/me